REMARKS

Status of claims

Claims 71-73 and 75-92 are currently pending in the application.

Claims 71 and 72 have been amended to recite an antibody or fragment thereof that binds to human c-kit "on a human hematopoietic cell line". The disclosure of human hematopoietic cell lines which display c-kit is found at p. 26, lines 5-10. These cell lines are also described at p. 9, lines 17-26 as being useful for producing antibodies of the present invention. It is believed that the amendments are fully supported by the specification and do not introduce new matter.

Rejection under 35 U.S.C. 112

Claims 71-73 and 75-92 are rejected under 35 U.S.C. 112, first paragraph, as the specification allegedly does not enable the subject matter of the claims. The Examiner relies on two lines of arguments: 1) The specification only contains a single working example of a monoclonal antibody (referred to in the specification as SR-1) which binds to human c-kit and prevents binding by stem cell factor. Citing *In re Fisher* 166 USPQ 18, 24 (CCPA 1970), the Examiner argues that the teachings of the specification pertaining to antibodies are narrow relative the scope of antibodies claimed and that there does not exist a reasonable correlation between the two; 2) The specification lacks objective evidence or working examples that the claimed antibodies could treat cancer, which the Examiner deems important in view of the alleged difficulties in treating solid tumors described in Curti (Crit. Rev. in Onc/Hematol. 14, 29-39 (1993)) and Jain (Sci. Am. 271, 58-65 (1994)) and the role of c-kit in the development of human tumors (Lennartsson et al. Curr. Cancer Drug Targets 6, 65-75 (2006)). Applicants disagree and request that the rejections be withdrawn.

The specification enables the full scope of the claimed antibodies

The specification clearly teaches how to make antibodies which bind human c-kit and block binding of human stem cell factor to human c-kit. In Example 1 of the specification, it is stated that "any cell displaying SCF receptors [c-kit] could be used as an immunogen to elicit antibodies to the SCF receptor [c-kit]" (p. 30, lines 12-13)

and a list of exemplary cells and cell lines is provided. The cells and cell lines referred to in the application were available from public depositories such as the American Type Culture Collection or could be prepared using commonly known techniques. Procedures for preparing and screening hybridomas which produce antibodies that bind to human c-kit were routine in the art at the time. In addition, an assay to determine whether a given c-kit antibody will inhibit binding of stem cell factor to c-kit is described in Example 5. It is clear that the specification teaches one to make and test antibodies other than SR-1 in order to identify those that bind human c-kit and inhibit the binding of stem cell factor.

As part of a review of the prior art, the Examiner refers to the following statement at p. 2, line 15 of the specification:

> ... until the existence of the present invention, the prior art had not been able to obtain a monoclonal antibody to the c-kit receptor with any expectation that such a monoclonal antibody would possess the ability to block the binding of the c-kit ligand, SCF.

Although there had been no previous reports of antibodies raised against c-kit which blocked SCF binding, this fact by itself does not mean that Applicants must be restricted to only their specific antibody. In fact, having taught for the first time a c-kit antibody which blocks SCF binding, Applicants' disclosure allows one to make additional antibodies.

In Ashman et al. (J. Cell. Physiol. 158, 545-554 (1994)), it was noted by the Examiner that the SR-1 antibody of the present application blocked the binding of SCF to c-kit while two other c-kit antibodies, YB5.B8 and 17F11, did not. The SR-1 antibody was reported to recognize a different epitope on c-kit from those recognized by the YB5.B8 and 17F11 antibodies, which likely accounted for the ability of SR-1 to block SCF binding. This, of course, is not evidence of lack of enablement but simply a recognition that antibodies raised against a particular target protein may have different binding epitopes which can result in different properties. It was routine in the art to find antibodies which recognize different epitopes on the same target and as a consequence have different activities.

The Examiner has not pointed out why one skilled in the art following the specification would require undue experimentation to make and use the claimed

antibodies. Instead, the rejection focuses on the presence of a single working example in the specification along with unsupported allegations that there is a lack of direction and guidance for preparing other antibodies which bind human c-kit and inhibit binding of stem cell factor. The review of the prior art merely showed that previous c-kit antibodies did not block SCF binding. As stated in *In re Wands* (8 USPQ2d 1404 (Fed. Cir. 1988)) one reaches a conclusion of undue experimentation based on consideration of all factors relating to undue experimentation. Applicants maintain that the direction and guidance set forth in the specification, the high level of skill in the art, and the existence of well known methods for practicing the invention point to substantial evidence of no undue experimentation. It is believed that the Examiner has not established a *prima facie* case of lack of enablement of the claimed antibodies or, in the alternative, that the *prima facie* case has been rebutted by Applicants.

The specification enables the use of c-kit antibodies to treat solid tumors and leukemia

None of the references concerning the role of c-kit in cancer provide any evidence that targeting c-kit with an antibody in the claimed methods would require undue experimentation. The "somewhat ambiguous" role of c-kit in cancer mentioned in the Lennartsson reference appears to be due to the loss of c-kit expression when certain tumors progress to a malignant phenotype. However, this statement does not rule out that the ability of an antibody to c-kit to treat certain cancers prior to becoming malignant. At most, Lennartsson et al. suggests that not all tumors express c-kit all the time. However, this does not establish that the use of a c-kit antibody to treat cancer is not enabled since absolute predictability is not required. The Lennartsson reference as a whole clearly indicates that targeting c-kit is a promising approach in a variety of cancers.

The Curti and Jain articles are general references that describe theoretical problems with the delivery of cytotoxic agents or biologics to tumors but do not describe any actual example of antibody therapy. Both articles refer to the relatively large size of an antibody and the potential problems associated with treating solid tumors with an antibody (see, for example, Jain at p. 63, col. 2). Nonetheless, one skilled in the art confronted with such a problem would have used antibody fragments having a smaller molecular weight to allow for more rapid penetration of

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the tumor. In fact, Curti states that a modeling approach predicts that smaller molecules, such as Fab fragments reach higher concentrations within a tumor than IgG (Curti at p. 36, left hand column). Antibody fragments were known in the art and recombinant DNA techniques described at p. 8, line 21 to p. 9, line 16 provide methods for manipulating variable heavy and light chain regions and CDRs to facilitate the construction of antibody fragments for cancer therapy.

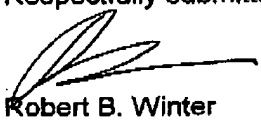
In view of the remarks above, it is believed that the rejection should be withdrawn.

CONCLUSION

It is believed that Claims 71-73 and 75-92 are in condition for allowance and a notice thereof is solicited.

The Commissioner is hereby authorized to charge any fees, which may be required by the accompanying papers, or credit any overpayment to Deposit Account No. 01-0519.

Respectfully submitted,



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